were validated in the context of alchemical free energies using several protein-ligand complexes.

804-Pos Board B584
LOOS: A Tool for Making New Tools for Analyzing Molecular Simulations
Tod D. Romo, Alan Grossfield.
Biochemistry & Biophysics, University of Rochester Medical School, Rochester, NY, USA.
We have developed LOOS (Lightweight Object Oriented Structure-analysis) as a tool for making new tools to analyze molecular simulations. LOOS is an object-oriented library designed to facilitate the rapid development of new methods for structural analysis. LOOS includes over 130 pre-built tools for common structural analysis tasks, including analyzing simulation convergence, 3D histograms, and elastic network models. LOOS supports reading the native file formats of most common simulation packages and can write NAMD formats (PDB and DCD) and Gromacs XTC. A dynamic atom selection language, based on C expression syntax, is included and is easily accessible via a single function call. LOOS is written in C++ and makes extensive use of Boost and the Standard Template Library. Through modern C++ design, LOOS is both simple to use (requiring knowledge of only 4 core classes and a few utility functions) and easily extensible. A Python interface to the core components of LOOS is also available, further facilitating rapid development of analysis tools and broadening the LOOS community by making it accessible to those who would otherwise be deterred by using C++. LOOS is available for download at http://loos.sourceforge.net

805-Pos Board B585
A Smoluchowski Equation for Force-Modulated Chemistry in Single Molecule Pulling Experiments
Gianmarc Grazioli, Ioan Andricioaei.
Chemistry, University of California, Irvine, Irvine, CA, USA.
Thioredoxins (Trx) are a class of enzymes, which catalyze the reduction of disulphide bonds between two cysteine residues, commonly found in proteins. An experimental investigation into the reaction mechanisms employed by various species of Trx was carried out by Perez-Jimenez et al. using single molecule force-clamp spectroscopy. The experiment involved applying a pulling force along the disulfide bond of the protein substrate, and measuring the rate of the Trx-catalyzed reduction as a function of the pulling force. One interesting finding of the experiment was that some forms of thioredoxin exhibit a biphasic relationship for reduction rate as a function of force magnitude. For this project, a mathematical model of this system was created, which employs a Smoluchowski formalism in the vein of Agmon-Hopfied or Sumi-Markus models. The model describes the time evolution of the probability distribution function of the protein's configuration within a space defined as the internal protein coordinate, as it diffuses over a potential which distorts under the applied force, while losing probability density to the Bell model type ''sink'' term, which is also a function of the applied force, representing reactants going to products (disulphide bond cleavage). By numerically solving the Smoluchowski equation and integrating the resulting surface over both time and the protein coordinate to calculate lifetime for increasing values of applied force, the model successfully reproduced the experimentally observed values for disulphide bond reduction rate as a function of applied force. Parameterizing the Smoluchowski equation to fit the experimentally measured data points provided a means of drawing insights into a physical interpretation of the model including the relationship between degree of biphasic behavior and the distance along the reaction coordinate from the bottom of the reactant well to the top of the transition state.

806-Pos Board B586
CHARMM-GUI Martini Maker for Coarse-Grained Simulations
Yifei Qi, Xi Cheng, Wonpil Im.
Department of Molecular Biosciences, Center for bioinformatics, Lawrence, KS, USA.
Coarse-grained simulations are widely used to study large biological systems. We have developed CHARMM-GUI Martini Maker for building solution, micelle, bilayer, and vesicle systems using Martini, a coarse-grained force field for biological molecules such as lipids, proteins, and carbohydrates. The supported force field includes martini, martini with polarizable water, dry martini, and ElNeDyn (an elastic network model for proteins). The qualities of the output systems are validated by simulation of various examples and comparison of the coarse-grained simulations to all-atom simulations. We expect this module to be a useful tool for modeling large, complicated systems in a user-friendly way.

807-Pos Board B587
Necessity of High Physical Resolution in the Development of Flexible Coarse-Grained Protein Models
ZhiGuang Jia, Jianhan Chen.
Biochemistry & Molecular Biophysics, Kansas State University, Manhattan, KS, USA.
The Martini force field is a one of the most widely used coarse-grained (CG) model. An important strength of the Martini force field is that it includes explicit, microscopic representation of solvent, which allows proper description of the context-dependence of protein-protein interactions. However, in the Martini force field the secondary structures of the protein are fixed, which makes it is unsuitable for simulating dynamic processes such as protein folding and membrane insertion. In this work, we examine the possibility of developing a flexible protein model within the Martini CG framework, such as by supplementing the force field with Go-like potentials. It was found the current Martini CG representation of proteins was insufficient to support a flexible model. The model does not provide a sufficient resolution to properly describe the volume and packing of protein backbone and sidechains. The interior voids resulting from improper packing would lead to excessive structural collapse in absence of structural restraints. Along this line, we further examined the PACE model, where an atomistic protein model is deployed in the Martini solvent. The results suggest that, while atomistic protein representation does dramatically improve the ability to describe specific protein-protein interactions, the low physical resolution of the Martini water molecules does not allow sufficient discrimination of various open and compact conformational states. As a result, PACE is not capable of describing context dependent protein structure transition, such as helical transition induced by membrane absorption and/or insertion. In conclusion, high physical resolution is likely necessary for developing flexible protein models and the coarse-graining needs to focus on exploiting possible simplification of interaction potentials.

808-Pos Board B588
Refining Multi-Scale Enhanced Sampling for Simulating Disordered Protein Conformations
Kuo Hao Lee, Jianhan Chen.
Department of Biochemistry and Molecular Biophysics, Kansas State University, Manhattan, KS, USA.
In the recently developed multiscale enhanced sampling (MSES) technique, topology-based coarse-grained (CG) models are coupled to atomistic protein force field to enhance the sampling of atomistic conformational space (Zhang and Chen, J. Chem Theory Comput, 2014). Here, we further refine the MSES protocol by designing more sophisticated Hamiltonian/temperature replica exchange schemes to more carefully control how the conformations are coupled between the atomistic and CG models, with a specific focus on optimizing the protocol for simulating disordered protein conformations. Preliminary results show that the new MSES protocols are effective in achieving better convergence in simulation of so-called intrinsically disordered proteins.

809-Pos Board B589
Investigation of a Method to Efficiently Create Elastic Networks
Patrick M. Diggins[1], Changjiang Liu[2,3], Raffaello Potestio[4], Markus Deserno[1].
[1]Physics, Carnegie Mellon University, Pittsburgh, PA, USA, [2]School of the Gifted Young, University of Science and Technology of China, Hefei, China, [3]Department of Physics, Carnegie Mellon University, Pittsburgh, PA, USA, [4]Max Planck Institute for Polymer Research, Mainz, Germany.
Elastic Networks (EN) have proven useful in the study of proteins, where they have a wide range of applications, from modeling the normal mode fluctuations of a protein to amending coarse grained (CG) force fields in order to conserve secondary and tertiary structures. In this project, we investigate the effectiveness of a systematic method for coarse-graining a protein (or part of a protein) into an EN where a substantial fraction of the particles are removed. The method begins with the creation of a Gaussian Network Model (GN) from either a high resolution EN or an all atom protein reference conformation and force field. By virtue of the GN being quadratic, we can analytically integrate out any number of degrees of freedom to create a CG GN with the same free energy as the original GN. Unfortunately, we cannot exactly transform the CG GN back to an EN because the GN no longer represents only central force interactions between particles. However, we can approximate the GN using an EN where the accuracy of the EN depends on the choice of particles that are removed. We show that a judicious choice of the configuration can significantly improve the accuracy of the EN. We discuss the ability of different optimization processes to efficiently find an optimum choice of the remaining particles. Finally, we investigate how well the resulting EN can replicate observables from the original system.